REMARKS / ARGUMENTS

Upon entry of this response, the pending claims are claims 10, 11, 23, 24, and 34, as previously amended.

35 U.S.C. § 112, first paragraph

> The Examiner has rejected claims 10, 11, 23, 24, and 34 under this paragraph for not fulfilling enablement requirements. The Examiner alleges the instant invention is enabled only for methods of treating or alleviating type 2 diabetes in a patient by administering compositions comprising antibodies directed to resistin polypeptides of SEQ ID NO: 2 and SEQ ID NO: 4, wherein said patient *is a mouse*. The Examiner's alleges that undue experimentation would be required to enable the instant invention for the treatment of patients other than mice.
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> The Examiner relies on publications such as Lee *et al*, J. Clin. Endocrin. Met., **2003**, 88(10):4848-4856; Heilbronn *et al*, J. Clin. Endocrin. Met., **2004**, 89(4):1844-1848; de Courten *et al*, Diabetes, **2004**, 53:1279-1284; and Iqbal *et al*, Eur. Rev. Med. Pharmacol. Sci., **2005**, 9:161-165 to assert that resistin levels in humans do not correlate with insulin resistance, thus serum glucose levels, and that the claimed method is unpredictable and requires undue experimentation.

Applicant respectfully disagrees with the Examiner and requests reconsideration and withdrawal of all outstanding rejections in view of the following remarks and the attached Declaration under 37 CFR 1.132.

Applicant's specification does comply with the enablement requirement in all respects.

As acknowledged by the Examiner, the specification is enabled for methods of treating or alleviating type 2 diabetes by administering compositions comprising antibodies directed to resistin using an animal model, i.e., a murine model. The use of this animal model is sufficient to support these teachings in a human. Applicant's data in the specification supports the role of resistin in methods of treating or alleviating type 2 diabetes. Relevant data in the specification includes both *in vitro* data and *in vivo* data.

In this original above-identified patent application specification, the role of resistin in methods of treating or alleviating type II diabetes was demonstrated by *in vitro*

data and *in vivo* data performed in mouse models. In the specification at page 112, lines 18-30 to page 113, lines 1 to 10, an experiment is described demonstrating the neutralization of resistin in a culture of 3T3-L1 mouse adipocytes to which anti-resistin antiserum or preimmune control serum was added. The basal uptake and insulin-stimulated uptake of radiolabeled 2-deoxyglucose were assessed for each cell culture. In contrast to little result with control serum, glucose uptake was markedly, approximately 250-300%, enhanced with the addition of anti-resistin antibodies (page 113, lines 4-5; Figure 20).

In further support of the role of resistin in methods of treating or alleviating type II diabetes, *in vivo* data in the specification demonstrates that resistin impairs glucose tolerance (page 113, lines 12-30 to page 114, lines 1-2). Specifically, female mice were treated with either vehicle or resistin. Upon treatment with purified resistin, experimental subjects treated with resistin had a significantly higher baseline blood glucose level than vehicle-treated mice, which is consistent with the diabetogenic effect of resistin (page 113, lines 22-24). Glucose tolerance was further exacerbated by glucose challenge, where vehicle-treated experimental subjects had a blood glucose level of 232 +/- 39 mg/dL and resistin-treated experimental subjects had a blood glucose level of 395 +/- 67 mg/dL 30 minutes following glucose administration (page 113, lines 25-30; Figure 21). These data observed in a mouse model demonstrated that resistin has a diabetogenic effect and that altering resistin concentrations *in vivo* represents a viable therapeutic option for treating or alleviating type II diabetes.

The invention of the pending claims for a method for treating type 2 diabetes is clearly enabled for human species by the use in the specification's examples of murine resistin in the mouse model.

Patentability can be found even when there is no true "working" example.[1] In this case, the specification does provides a true "working" example, albeit in an animal model. As such, the instant invention clearly meets the requirement for guidance and examples in respect to patentability. The model should be accepted unless the examiner has evidence that the model does not correlate. "Even with such evidence, the examiner ***must*** weigh the evidence ***for and against*** correlation and decide whether one skilled in the art would accept the model as ***reasonably*** correlating to the condition", MPEP 2164.02 (emphasis added), and further supported by *In re Brana*, 51 F. 3d 1560, 1566 (Fed Cir 1995).

In evaluating whether or not the specification enables the claimed treatment to extend to treatment of humans, the Examiner must weigh the evidence *in toto* to determine if a person of ordinary skill in the art would find the invention as demonstrated in the murine model, but directed to the treatment of humans, to be enabled or not. Furthermore the evidence provided by the Applicant "need not be conclusive but merely convincing to one skilled in the art."[2]

The evidence required for the purposes of enablement in the instant case would be sufficient if it can be shown that there is a reasonable correlation between the mouse model and the human condition. Applicant asserts that the correlation between these mouse and human uses would be accepted as reasonable despite the citations provided by the Examiner for the following reasons for the reasons outlined in the inventor's Declaration.

As indicated in the inventor's Declaration, the publications cited by the Examiner are not evidence that the specification is non-enabling. The existence of purportedly conflicting reports in the art regarding the relationship between human resistin and insulin resistance and type 2 diabetes is not sufficient to render the instant invention non-

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[1] An example may be "working" or "prophetic." . . . A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved.

[2] MPEP § 2164.05.

enabled and consequently unpatentable. The publications relied on by the Examiner have alleged that human resistin is possibly **not** correlated to obesity or insulin resistance. However, each of these cited documents sets forth cautionary remarks regarding their conclusions and findings.

The inventor's Declaration points out that these documents do not form a majority consensus on this issue. The conclusions reached by these documents are not in agreement with conclusions reached by other documents that support the role for the use of resistin in human type 2 diabetes. Some combination of sample size, population being studied, assay employed and actual performance of the assays may be related to the conclusions of these references and why their conclusions differ with those of the authors of other studies.

Other publications support the Applicant's contention that resistin (murine or human) does correlate with type 2 diabetes in humans. The inventor's attached Declaration draws the Examiner's attention to publications by a number of other researchers, who have established that resistin is significantly correlated with type 2 diabetes in humans. These documents are cited in the Supplemental Information Disclosure Statement, filed herewith. Thus, the weight of the scientific evidence to date is submitted to support the conclusions drawn in the original specification that human resistin, like mouse resistin, has a diabetogenic effect, at least in some populations of humans, and that altering resistin concentrations *in vivo* using an anti-resistin antibody represents a viable therapeutic option for treating or alleviating type 2 diabetes in populations demonstrating this effect.

The documents cited in the Declaration and provided in the supplemental IDS thus support the predictability of the claimed invention and demonstrate that undue experimentation would <u>not</u> be required to enable one of skill in the art to practice this invention.

In view of the foregoing remarks and the inventor's Declaration, the Applicant respectfully requests that the Examiner reconsider and withdraw all outstanding rejections and permit the above pending claims to pass to issue in due course.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to Deposit Account Number 08-3040.

Respectfully submitted,

HOWSON AND HOWSON
Attorneys for Applicant

By _____
Mary E. Bak
Registration No. 31,215
501 Office Center Drive
Suite 201
Fort Washington, PA 19034
Phone: (215) 540-9200
Fax: (215) 540-5818